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Original Article

A pilot outreach physiotherapy and dietetic quality improvement initiative reduces IV antibiotic requirements in children with moderate–severe cystic fibrosis

Sean J. Ledger [a, e,*], Elizabeth Owen [b], S. Ammani Prasad [a], Allan Goldman [c], Jane Willams [d], Paul Aurora [a, e]

[a] Cystic Fibrosis Unit, Great Ormond Street Hospital for Children NHS Foundation Trust, London, United Kingdom
[b] Dietetic Department, Great Ormond Street Hospital for Children NHS Foundation Trust, London, United Kingdom
[c] Cardiothoracic Department, Great Ormond Street Hospital for Children NHS Foundation Trust, London, United Kingdom
[d] Childhood Nutrition Research Centre, University College London Institute of Child Health, London, United Kingdom
[e] Portex Respiratory Unit, University College London Institute of Child Health, London, United Kingdom

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Abstract

Background: At our hospital the current model of care for children with moderate–severe CF is focused on intensive inpatient intervention, regular outpatient clinic review and specialist outreach care as required. An alternative model providing more regular physiotherapy and dietetic outreach support, in addition to these specialist services, may be more effective.
Methods: 16 children (4 male; 12 female; mean age 10.9±2.93; range 4–15 years) who required >40 days of IV antibiotics in the 12-months pre-intervention were enrolled. Physiotherapy included weekly-supervised exercise sessions, alongside regular review of home physiotherapy regimens. Dietetic management included 1–2 monthly monitoring of growth, appetite, intake and absorption, and nutrition education sessions.
Results: There was a 23% reduction in inpatient IV antibiotic requirement and 20% reduction in home IV antibiotic requirement during the intervention year. Cost–benefit analyses showed savings of £113,570. VO_{2Peak} increased by 4.9 ml·kg·min^{-1} (95%CI 1.01 to 8.71; p=0.02), and 10 m-MSWT distance and increment achieved increased by 229 m (95%CI 109 to 350; p<0.001) and 2 levels (95%CI 1 to 3; p<0.002) respectively. No significant differences in physiological and patient reported outcomes were demonstrated, although there was a possible trend towards improvement in outcomes when compared to the pre-intervention year.
Conclusion: This pilot programme demonstrated a reduction in IV and admission requirements with a cost benefit in a small group of children with moderate–severe CF. A fully powered clinical trial is now warranted.

Keywords: Exercise; Physiotherapy; Dietetics; Cystic fibrosis

1. Introduction

Regular exercise may help to maintain or increase lung function [1] and increase the effectiveness of airway clearance techniques in children with cystic fibrosis (CF) [2]. It may also improve aerobic capacity, muscle strength and lung function [3]. However, it is important to carefully monitor growth and body composition in children who regularly exercise, as increased energy demands may impact on body mass index (BMI) that is strongly correlated with lung function [4].

Two previous observational studies in small groups of children with moderate–severe CF, one presented in abstract format [5] and the other recently published [6], reported that a 12-month intensive outpatient physiotherapy and exercise programme significantly

* Corresponding author at: Cystic Fibrosis Unit, Great Ormond Street Hospital for Children NHS Foundation Trust, Great Ormond Street, London, WC1N 3JH, United Kingdom. Tel.: +44 20 7405 9200x1119; fax: +44 20 7813 8514.
E-mail address: sean.ledger@gosh.nhs.uk (S.J. Ledger).

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reduced requirements for intravenous antibiotic (IV) treatment and also increased exercise capacity.

The 12-month pilot Frequent Flyer Programme (FFP) was undertaken as a quality improvement initiative within the CF Unit of Great Ormond Street Hospital for Children (GOSH), in addition to the specialist services already provided. The purpose was to try and replicate these positive results and to determine feasibility for a larger controlled trial. The investigators hypothesised that reduced inpatient admissions would benefit the children and be economically advantageous to the hospital. Additionally, increased exercise capacity may help to maintain or increase lung function. A dietetic component was included to monitor for changes in growth and energy requirements as a result of increased exercise.

This was a pragmatic clinical intervention, targeted at a specific population, so a pre-intervention power calculation was not performed, and there was no blinding of clinicians involved with the programme. Weekly outreach physiotherapy and more regular nutrition support were provided to a small group of children who required multiple courses of IV treatment in the previous year. The primary outcome was the total number of IV days required in the 12-month intervention period, compared to 12-months pre-intervention. A cost-analysis was also undertaken. Secondary outcomes included exercise capacity, lung function, growth and body composition, and quality of life (QoL) assessment.

2. Methods

A top-down approach was applied, such that children from the GOSH CF cohort (n = 178) with the most IV requirements in the pre-intervention year were enrolled first on the programme. Children were identified by retrospective analysis of the previous year's admission data. Inclusion criteria were a confirmed diagnosis of CF, aged 4–15 years, with a baseline $FEV_1 > 30\%$, and a requirement of > 40 days of IV treatment in the 12-months pre-intervention. No microbiological exclusion criteria were set.

The Chairman of the GOSH Ethics Committee confirmed that a full ethics review was not required, nevertheless written information was given and verbal consent to participate was obtained from parents or guardians, and children where appropriate.

2.1. Requirement for admissions for routine IV

All participants had pre-scheduled, 3–4 monthly admissions for routine IV treatment; however, respiratory exacerbations and bed pressures regularly affected these dates. Requirement for admission was assessed at an outpatient clinic 2–4 weeks prior to routine admissions. The attending consultant could make a clinical decision to bring forward a symptomatic child's admission, or children maintaining or showing improvement in clinical status could have their admission delayed. Participants were typically admitted to GOSH, however, some children were admitted to their local hospital if part of the GOSH shared-care network.

2.2. Outcome measures

2.2.1. IV and inpatient days

The total number of inpatient IV treatments administered at GOSH, shared-care hospitals and for IV courses completed at home, during the 12-months pre-intervention was documented for each child at baseline. Data for the intervention period were collated post-intervention.

Physiological and exercise outcome measurements recorded during times of clinical stability (i.e. not during an exacerbation, not on steroids, and not during or within 2 weeks of IV treatment) for 1-year pre-intervention, baseline and post-intervention were used for analysis.

2.2.2. Cardiopulmonary exercise testing

Cardiopulmonary exercise testing (CPET) was performed at baseline to identify exercise-induced limitations and provide parameters for individualised exercise prescription. It was repeated post-intervention to assess changes in aerobic capacity. A Godfrey cycle protocol was performed at each session [7], with continuous respiratory gas analysis (Medgraphics, St. Paul, Minnesota), electrocardiography and oxygen saturations (S_pO_2) monitoring. Participants were encouraged throughout the tests to make a maximal effort. The test was considered maximal when the participant achieved one of the following: 1) heart rate > 90% age-predicted maximum; 2) respiratory exchange ratio (RER) ≥ 1.05; or 3) a peak minute ventilation (V_E) close to predicted target [8,9]. Children aged < 6 years, or those that did not meet the minimum 120 cm height requirement at baseline to sit safely on the ergometer bike, were excluded from CPET. Additionally, those infected with *methicillin-resistant Staphylococcus aureus* (MRSA) or *Burkholderia cepacia* were excluded due to infection control risks.

2.2.3. 10m modified shuttle walk test

The 10m modified shuttle walk test (10m-MSWT) was performed at baseline and post-intervention to assess functional exercise capacity [10,11].

2.2.4. Lung function

Spirometry (Erich Jaeger AG, Wurzburg, Germany), height (Holtain Ltd, Dyfed, UK) and weight (Seca, Birmingham, UK) were measured at baseline, regularly during the 12-month intervention period, and post-intervention. Spirometry was performed according to GOSH laboratory standards, which are based on ERS/ATS guidelines [12].

2.2.5. Growth and body composition

Body composition measurements were performed at baseline and post-intervention. Left sided, mid-upper arm circumference (MUAC) [13] and the mean of three measurements of biceps, triceps and subscapular skinfold thickness (SFT) (Holtain Ltd, Dyfed, UK) were used to estimate fat mass [14]. Using a previously described method [15], deuterium dilution techniques were used as a proxy for calculating lean mass, and were analysed by Iso-Analytic Ltd (Sandbach, UK).

2.2.6. Patient and parent reported outcomes

The Cystic Fibrosis Questionnaire UK version (CFQ) [16] was completed at baseline and post-intervention to evaluate changes in QoL. Children aged ≥14 years used the self-assessed CFQ-14+ version, whilst those aged 6–13 used age appropriate clinician assisted versions. Children and parents completed a satisfaction questionnaire post-intervention.

2.3. Intervention

2.3.1. Physiotherapy

The physiotherapist used FEV_1, CPET and 10m-MSWT results to prescribe an age appropriate, individualised exercise programme. Exercise training compromised of high intensity interval training using cardiovascular training equipment (e.g. treadmill, bike, and cross-trainer) interspersed with periods of recovery. This allowed for recovery from breathlessness, and huffing and coughing was performed to facilitate airway clearance. Strength, core-conditioning and stretching components were also included. Children with a baseline $FEV_1 > 70\%$ exercised for 45–60 min, of which 20–30 min was at 70–85% of maximum heart rate (HR_{Max}), whilst children with a baseline $FEV_1 = 39–69\%$ exercised for 30–45 min for 15–25 min at 60–80% HR_{Max}. HR_{Max} was monitored by portable Nonin 2500 S_pO_2/HR monitors (Nonin Medical Inc., Plymouth, USA). In addition, children were also encouraged to exercise independently, and actively participate in school PE lessons and sport for an additional 2 hours per week. Free membership to a local fitness facility was negotiated for each of the children, at which the physiotherapist supervised weekly training sessions.

Home physiotherapy regimens were reviewed monthly to reinforce optimal airway clearance and mucolytic inhalation therapy. When parents reported an exacerbation of respiratory symptoms, the physiotherapist would assess the child at home or clinic, escalate home physiotherapy treatment and collect a sputum sample. The physiotherapist would also coordinate with the multidisciplinary team (MDT) when a course of oral antibiotics was necessitated.

2.3.2. Dietetics

Increased input from the dietitian included a minimum of 1–2 monthly monitoring of weight. Assessment of appetite, intake, and absorption was through verbal consultation telephonically, at clinics, during inpatient admissions and occasional home visits. Focus was on the child's response to exercise with additional calorie supplementation prescribed when needed. The dietitian reviewed oral supplements, enteral feeds, vitamins, enzyme administration and dosage. Educational resources were developed and individualised nutrition sessions were delivered to the child about pancreatic enzyme therapy, energy requirements, and vitamin and mineral needs.

2.4. Statistical analysis

Data were entered into a Microsoft Excel database and statistical analyses were undertaken using IBM® SPSS® Statistics 21 (Chicago, IL, USA). Lung function [17], weight, height, BMI [18,19] and body composition [20], results were converted to z-scores. A repeated measures test was used to compare pre-intervention, baseline and post-intervention data. Paired t-tests were used to compare data at baseline and post-intervention only. Data were expressed as mean±standard deviation (SD), 95% confidence intervals (CI), and an alpha level of 0.05 was established for statistical significance.

2.5. Healthcare cost analysis

Cost analyses were completed post-intervention. Two methods were used to evaluate the cost implications of the programme. First, a comprehensive internal cost analysis determined that the cost per day for GOSH inpatient admissions for this cohort were approximately £1210 per day. Internal cost analysis was calculated on audited MDT staffing costs; cost of blood, radiological and pathology tests; drug expenses; device and clinical support expenses; and theatre and ward expenses. Home IV costs were calculated at £168 per day based on costs provided by the supplier, Willow Healthcare Services UK. Second, the published generic National Health Service (NHS) unit reference costs for a paediatric hospital bed are approximately £658 per day [21]. Shared-care inpatient costs were determined using NHS unit costs, as full internal costing was impractical.

Setup-cost for the programme was £100,000 to include a full-time physiotherapist, part-time dietitian, lease of vehicle, road-tax and diesel costs. Children in this programme availed of a free gym membership. However, other centres implementing this type of intervention may have to consider the cost of gym memberships in setup-costs. Personal communication with these facilities determined cost per membership for a child ranged between £15 (local council leisure centre) to £52 (nationwide health and wellbeing centre) per month. Cost–benefit analysis included these potential costs.

3. Results

3.1. Participants

Twenty children were eligible to participate. Two children received lung transplantation before baseline data was collected and were therefore not enrolled. One child did not wish to participate and one child was excluded due to pre-existing social concerns.

Sixteen children (4 male) aged 4–15 years (10.9±2.93) started the programme. All, but two, completed the programme; one child relocated and one died midway through the programme. Both were excluded from final analysis. Nine children were homozygous for the ΔF508 genotype and all, except 1, had pancreatic insufficiency. This child was excluded from growth and body composition analysis, as dietetic requirements and management were very different to the pancreatic insufficient children. One child received maxillofacial surgery in the last month of the programme and therefore did not complete CPET or body composition measurement post-intervention. Descriptive baseline demographics are presented in Table 1.

3.2. IV requirements

There was a 21% reduction in the requirement for GOSH inpatient IV treatment, from 619 days in the pre-intervention year to 478 in the intervention year; a 24% decrease in shared-care inpatient IV requirement from 249 to 189 days; and a 20% reduction in home IV treatment from 304 to 243 days. The overall 22% reduction in IV requirement represented a substantial reduction when compared to pre-intervention data (Table 2).

3.3. Healthcare costs

Full internal cost analyses (Table 3) determined there was an estimated saving of £170,610 in GOSH inpatient costs; £39,480 in shared-care hospital bed costs; and £10,248 in home IV costs. Average cost per patient during the pre-intervention year was £60,244 compared to £46,472 in the intervention year demonstrating a mean cost saving per patient of £13,772. An alternative cost analysis, employing generic NHS bed costs only, is detailed in the online supplement.

After factoring in the £100,000 set up costs for the programme, plus estimated annual gym memberships costs of £6768, the average cost per patient during the intervention year was £53,146 suggesting an overall cost saving of £7098 per patient or £113,570 overall.

3.4. Cardiopulmonary exercise testing

Thirteen children met the minimum requirements to perform CPET. Of these, one child refused to participate due to intolerance of the facemask, and one was not able to repeat the test as she had maxillofacial surgery. Post-intervention, paired t-tests showed a statistically and clinically significant increase in VO_{2Peak} of 4.9 ml·kg·min^{-1} (CI 1.0 to 8.7; p=0.02) and VO_{2Peak}%pred by 14% (CI 1.9 to 25.8; p=0.03*) (Table 4). All children maintained S_pO_2>95% during testing and no arrhythmias were detected.

Table 1
Baseline demographics for group.

Variable	Number
Male/female	4/12 (n=16)
Mean age±SD [range]	10.9±2.93 [4 to 14]
Genotype	ΔF508/ΔF508=9 ΔF508/other=5 Other mutations=2
Pancreatic insufficiency	15
CF related diabetes	1
Impaired glucose tolerance	1
Indeterminate glycaemia	1
Microbiology	
Chronic *Pseudomonas aeruginosa*	10 (63%)
Chronic *Staphylococcus aureus*	1 (1%)
Chronic methicillin-resistant *Staphylococcus aureus*	1 (1%)
History of allergic bronchopulmonary aspergillosis	5 (31%)
History of nontuberculous mycobacteria	3 (19%)

Table 2
IV antibiotic day requirement for 12-months pre-intervention and post-intervention.

Venue (no. of patients)	Total pre-intervention	Total post-intervention	Total diff. (mean diff)
GOSH IV days (16)	619 (39±27)	478 (30±37)	−141 (−8.8)
Home IV days (7)	304 (43±18)	243 (35±15)	−61 (−8.7)
Shared care IV days (8)	249 (31±27)	189 (24±20)	−60 (−7.5)
Total (16)	1172 (73±25)	910 (57±41)	−262 (−16.4)

Data presented as total (mean±standard deviation).

3.5. 10 m modified shuttle walk test

Thirteen children completed 10m-MSWT; one child aged 5 was not tested. Paired t-tests showed a statistically and clinically significant increase in distance walked or run and number of increments achieved, by 229m (CI 108.8 to 349.7; p=0.001) and 2 levels (CI 0.8 to 2.6; p=0.002) respectively (Table 4).

3.6. Lung function

Repeated measure tests showed no statistically significant differences in FEV_1 z-scores over time. Mean FEV_1%pred for the group declined significantly by >9% (CI −17.1 to −1.1; p=0.02) in the pre-intervention year. Although non-statistically significant, the difference in rate of change between baseline to post-intervention and pre-intervention to baseline, FEV_1%pred had improved by almost 9% (CI −3.3 to 23.0; p=0.13). This may suggest a possible trend towards slowing the rate of decline. When converted to z-scores the results suggest a similar trend. Physiological data are presented in Table 5.

3.7. Growth and body composition

At baseline, 3 children were classified as malnourished (BMI<15th percentile) [22]. Two children (both female) had a gastrostomy in situ and 10 children were receiving oral calorie supplements. Repeated measure tests showed no statistically significant differences in growth parameters. Changes in BMI and lean mass z-scores are graphically presented in the online supplement.

Ten children maintained a BMI z-score within 0.5 of their baseline measurement during the intervention. One child who was categorised as malnourished at baseline increased their BMI z-score by 0.5 post-intervention. However, 2 children with good baseline nutritional status showed a decline >0.5 in BMI z-score post-intervention. Similar trends were noted for weight. Post-intervention 7 children were taking oral supplements; 4 were taking increased amounts including one child who was referred for a gastrostomy, and 2 used occasional oral supplements.

Twelve children completed deuterium dilution testing, MUAC and SFT measurements. Paired t-tests showed no statistically significant changes in lean mass and MUAC z-scores. There was a statistically significant increase of 0.4 (CI 0.2 to 0.7; p=0.001) in the aggregated group SFT z-scores. Five children (2 pubertal boys, 1 pubertal girl and 2 pre-pubertal girls) increased their lean mass z-scores (range 0.01 to 0.3); however, as a group, there was

Table 3
Cost analysis for 12-months pre-intervention and post-intervention.

Cost; number of patients	Total cost pre-intervention (mean±SD)	Total cost post-intervention (mean±SD)	Total cost difference (mean cost diff)
Daily GOSH [a] admission cost approx. £1210 [a], n=16	£748,990 (46,812±33,054)	£578,380 (36,149±44,319)	−£170,610 (−10663)
Daily cost of home IV-antibiotic treatment approx. £168; n=7	£51,072 (7,296±3,005)	£40,824 (5,832±2,542)	−£10,248 (−1464)
Daily cost of shared care hospital bed approx. £658; n=8	£163,842 (20,480±17,675)	£124,362 (15,545±13,430)	−£39,480 (−4935)
Total cost of hospital admission and home IV treatment; n=16	£963,904 (60,244±29,556)	£743,566 (46,472±48,696)	−£220,338 (−13,772)
Total cost plus setup costs [b] and gym membership cost [c]; n=16	£963,904 (60,244±29,556)	£850,334 (53,146±48,641)	−£113,570 (−7098)

Data presented as Total (mean±standard deviation).
[a] GOSH internal cost analysis was calculated on audited MDT staffing costs; cost of blood, radiological and pathology tests; drug expenses; device and clinical support expenses; and theatre and ward expenses.
[b] Total setup cost=£100,000.
[c] Estimated annual gym membership costs=£6768 [Range £15–£52].

a non-statistically significant decrease of 0.2 in lean mass z-scores.

3.8. Patient reported outcomes

There was a non-statistically significant increase of 1.3% in total CFQ scores from 71% to 72.3% for the group. Graphic representation of CFQ scores and further discussion are presented in the online supplement. The results of the end of programme evaluation questionnaires showed that patients (76%) and parents (79%) highly rated both the physiotherapy and dietetic components of the programme. All said they would recommend this type of programme for other children with CF.

4. Discussion

The 12-month FFP demonstrated that intensive weekly outreach physiotherapy and exercise, and more frequent dietetic support can reduce requirements for IV treatment in a small group of children with moderate–severe CF. Cost savings were realised and exercise capacity was significantly increased.

The FFP was similar in structure to the two previous studies. Black et al. [5] demonstrated that in 10 children (mean age 13.2) with CF, IV requirement was reduced by 48%. Urquhart et al. [6] performed a similar intervention in 12 adolescent subjects (mean age 13.3), and demonstrated a 23% reduction in IV requirement; improved 10m-MSWT scores; and improved QoL scores. In addition, cost–benefit, using NHS generic estimates were calculated. The FFP realised similar decreases in IV requirement and increases in exercise capacity, with these increases being independent of lung function. The programme did not demonstrate changes in physiological or quality of life scores, although there were possible emerging trends of slowing the rate of lung function decline.

CPET was used for the first time in this small group to determine exercise capacity. Results demonstrated a significant increase of 13% in VO_{2Peak}%pred, suggesting a significant increase in aerobic exercise capacity. Importantly, participants who increased their level of cardiopulmonary fitness may have increased their chances of survival [23]. Every effort was made to standardise the test procedures, however it should be noted that CPET was new to these children. Maximal efforts were

Table 4
Exercise test data at baseline and post-intervention.

Outcome	Baseline	Post-intervention	Diff. baseline to post-intervention (95%CI; p-value)
CPET (n=11)			
VO_{2Peak}%pred in %	69.6±18.5	83.5±22.0	13.8 (1.9 to 25.8; 0.03 *)
VO_{2Peak} at anaerobic threshold (ml.kg.min^{-1})	20.0±7.2	21.8±8.8	1.8 (−2.9 to 6.5; 0.41)
VO_{2Peak} (ml.kg.min^{-1})	28.8±8.8	33.7±9.4	4.9 (1.0 to 8.7; 0.02 *)
HR_{Max} (BPM)	160.0±20.7	166.6±16.3	6.6 (−3.8 to 17.0; 0.19)
RER	1.06±0.12	1.06±0.12	0.00 (−0.04 to 0.05; 0.94)
VE/VCO_2	33.6±6.8	29.8±11.3	−3.8 (−13.3 to 5.8; 0.40)
VE BTPS (L/min)	37±18	49±22	12.1 (−0.35 to 24.5; 0.06)
VCO_2 (ml/min)	1165±515	1318±608	153 (−27 to 332; 0.08)
Pre-exercise S_pO_2	99.0±3.8	97.2±2.0	−1.7 (−4.3 to 0.9; 0.17)
S_pO_2 at VO_{2Peak}	100.3±4.9	96.9±3.6	−3.4 (−6.5 to −0.3; 0.4 *)
10 m-MSWT (n=13)			
Distance (m)	710±276	940±349	229 (108.8 to 349.7; 0.001 *)
Level	9±2	11±3	2 (0.8 to 2.6; 0.002 *)
HR_{Max} (BPM)	157.1±19.7	175.1±11.2	18 (7.1 to 28.9; 0.004 *)
Lowest S_pO_2	94.1±2.8	94.8±2.2	0.7 (−1.0 to 2.4; 0.3)
Peak breathlessness (Borg 1–10)	8±1.3	9±1	1 (0.3 to 1.6; p=0.008 *)

Data presented as mean±standard deviation.
* Statistically significant.

Table 5
Physiological data for 12-months pre-intervention, baseline and post-intervention.

Outcome	1-Yr pre-intervention	Baseline	Post-intervention	Diff. 1-yr pre-intervention to baseline (95%CI; p-value)	Diff. baseline to post-intervention (95%CI; p=value)	Diff. in rate of change between baseline to post-intervention and pre-intervention to baseline (95%CI; p=value)
Lung function (n=14)						
FEV1% predicted	76.6±20.9	67.3±26.0	67.9±21.0	−9.3 (−17.1 to −1.1; 0.02*)	0.6 (−7.4 to 8.6; 0.88)	8.7 (−3.3 to 23.0; 0.13)
FEV1 (L)	1.3±0.6	1.3±0.5	1.5±0.7	0.0 (−0.3 to 0.3; 0.87)	0.2 (−0.04 to 0.3; 0.12)	0.2 (−0.3 to 0.5; 0.53)
FEV1 z score	−2.7±1.6	−3.0±1.6	−3.1±1.6	−0.3 (−1.3 to 0.6; 0.50)	−0.1 (−0.6 to 0.4; 0.64)	0.2 (−1.1 to 1.5; 0.76)
FVC% predicted	87.6±16.8	80.6±21.8	82.1±17.1	−7.0 (−14.9 to 0.8; 0.08)	1.5 (−6.5 to 9.5; 0.69)	5.5 (−4.9 to 22.0; 0.19)
FVC (L)	1.7±0.7	1.8±0.6	2.1±0.8	0.1 (−0.3 to 0.4; 0.74)	0.3 (0.1 to 0.4; 0.008*)	0.2 (−2.3 to 0.6; 0.34)
FVC z-score	−1.8±1.7	−2.1±1.5	−2.0±1.43	−0.3 (−1.4 to 0.8; 0.51)	0.1 (−0.4 to 0.5; 0.78)	0.4 (−0.9 to 1.7; 0.53)
Growth (n=13)						
BMI z-score	−0.2±0.7	−0.3±0.7	−0.4±0.5	−0.1 (−0.5 to 0.2; 0.36)	−0.1 (−0.3 to 0.1; 0.35)	0.0 (−0.4 to 0.5; 0.87)
Weight z-score	−0.2±0.6	−0.5±0.6	−0.6±0.5	−0.3 (−1.5 to −0.00; 0.05*)	−0.1 (−0.3 to 0.0; 0.10)	0.2 (−0.3 to 0.4; 0.64)
Height z-score	−0.2±0.66	−0.4±0.7	−0.5±0.9	−0.2 (−0.3 to −0.04; 0.01*)	−0.1 (−0.2 to 0.08; 0.34)	0.1 (−0.04 to 0.28; 0.14)
Lean mass (n=12)						
Deuterium z-score (LMM)	–	−0.8±1.1	−1.0±1.0	–	−0.2 (−0.4 to 0.1; 0.18)	
Fat mass (n=12)						
Aggregated skin-fold z-score (FM)	–	−0.3±0.6	0.1±0.7	–	0.4 (0.2 to 0.7; 0.001*)	
MUAC	–	−0.8±0.7	−0.9±0.9	–	−0.1 (−0.5 to 0.2; 0.35)	

Data presented as mean±standard deviation.
* Statistically significant.

achieved, however, it may be possible that children knew what to expect and tried harder in the second test.

The 10m-MSWT was used to confirm the CPET results. Although significant increases in distance covered and incremental level achieved were demonstrated, an important potential confounder is that age and leg length increases may have contributed to the increased parameters in the 10m-MSWT when repeated at yearly intervals. Increased HR_{Max} measurements do suggest that exercise capacity had increased post-intervention. In both exercise tests, baseline HR_{Max} was lower than post-intervention, despite perceived maximal effort; we speculate this may be because children were less tolerant of breathlessness or less tolerant of exercising at a high intensity at baseline and may have stopped before HR_{Max} was achieved.

More frequent dietetic review enabled earlier identification of nutritional problems and allowed for dietary modifications to be made to address individual requirements. Children with poor baseline nutritional status and growth required closer monitoring. It is well documented [4,24–26] that many variables may affect growth in children with CF, including inadequate calorie intake, increased energy expenditure, malabsorption, and impaired glucose metabolism. The FFP demonstrated that it could be challenging to maintain steady growth in some children who exercise more, and some children reported an added burden of taking more supplements in response to higher energy requirements.

Notably, in the pre-intervention year, weight and height z-scores were significantly declining; however, post-intervention, although results did not reach significance, there was a trend for the rate of decline to slow. As with the spirometry data, this programme was not powered to assess this comprehensively and 12-months may have been too short a time period to demonstrate acceleration in growth for those children with poorer nutritional status.

With an increase in exercise it is important to address individual energy and nutritional requirements early, with longitudinal monitoring of growth and nutritional status. Despite regular strength training, lean mass did not increase. However as lean mass data was not recorded for the pre-intervention year, it is not possible to make comparisons with year on year data. Williams et al. [27] reported that females in particular have a lower fat mass than the reference population; this may explain why the predominantly female group in the FFP did not demonstrate improvements in lean mass.

As with the two previous studies, the FFP had a number of clear limitations, related to this being a report of an observational quality improvement initiative, rather than a designed intervention study, and as such is exposed to bias. In assessing the effect of the intervention, the pre-intervention year was used as the control sample rather than having separate controls. In addition, the sample size of the FFP was not powered to clearly demonstrate the benefit of this exercise intervention upon lung function. However, as the FFP has confirmed and extended the findings of the previous two studies, a fully powered randomised controlled trial is now warranted, and recruitment for the INSPIRE-CF trial has commenced.

The FFP demonstrated a reduction in IV requirement with a cost–benefit, and significant increases in exercise capacity, in this small cohort of sicker children with moderate–severe CF. If the positive results realised in this pilot programme were

replicated in other CF units across the UK, the implications for cost saving, improvement in clinical status and quality of life are potentially extensive.

Competing interests

None.

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Contributors

All co-authors have been closely involved in the programme since inception, have contributed to the manuscript, and have approved the final draft.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.jcf.2013.01.003.

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